

WO 01/09187

- 1 -

SEQUENCE LISTING

<110> Medarex, Inc.

<120> HUMAN MONOCLONAL ANTIBODIES TO HER2/NEU

<130> MXI-160PC

<140>

<141>

<150> USSN 60/146,313

<151> 1999-07-29

<150> USSN 60/188,539

<151> 1999-03-10

<160> 13

<170> PatentIn Ver. 2.0

<210> 1

<211> 372

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1) .. (372)

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Glu	Val	Gln	Leu	Leu	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly	
1				5					10					15		

tcc	ctg	aga	ctc	tcc	tgt	gca	gcc	tct	gga	ttc	acc	ttt	agc	agc	tat	96
Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Ser	Tyr	
		20						25					30			

gcc	atg	acc	tgg	gtc	cgc	cag	gct	cca	ggg	aag	ggg	ctg	gag	tgg	gtc	144
Ala	Met	Thr	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val	
		35					40					45				

tca	gct	atc	agt	ggt	agt	ggt	tat	agc	aca	tac	tac	gca	gac	tcc	gag	192
Ser	Ala	Ile	Ser	Gly	Ser	Gly	Tyr	Ser	Thr	Tyr	Tyr	Ala	Asp	Ser	Glu	
		50				55					60					

aag	ggc	cgg	ttc	acc	atc	tcc	aga	gac	aat	tcc	aag	aac	acg	ctg	tat	240
Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr	
		65				70				75				80		

ctg	caa	atg	aac	agc	ctg	aga	gcc	gag	gac	acg	gcc	gta	tat	tac	tgt	288
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Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95

Ala Lys Gly Phe Gln Tyr Gly Ser Gly Ser Tyr Tyr Thr His Phe Asp  
100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
115 120

<213> Homo sapiens

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
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Ala Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
35 40 45

Ser Ala Ile Ser Gly Ser Gly Tyr Ser Thr Tyr Tyr Ala Asp Ser Glu  
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95

Ala Lys Gly Phe Gln Tyr Gly Ser Gly Ser Tyr Tyr Thr His Phe Asp  
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Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
115 120

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<222> (1) .. (321)

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gac aga gtc acc atc act tgt cgg gcg agt cag ggt att agc agc tgg 96  
 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp  
 20 25 30

tta gcc tgg tat cag cag aaa cca gag aaa gcc cct aag tcc ctg atc  
 144  
 Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile  
 35 40 45

tat gct gca tcc agt ttg caa agt ggg gtc cca tca agg ttc agc ggc  
 192  
 Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly  
 50 55 60

agt gga tct ggg aca gat ttc act ctc acc atc agc agc ctg cag cct  
 240  
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro  
 65 70 75 80

gaa gat ttt gca act tat tac tgc caa cag tat aat agt tac ccg tac  
 288  
 Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Tyr  
 85 90 95

act ttt ggc cag ggg acc aag ctg gag atc aaa  
 321  
 Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys  
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 <211> 107  
 <212> PRT  
 <213> Homo sapiens

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Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile  
 35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly  
 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro  
 65 70 75 80

- 4 -

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Tyr  
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Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys  
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&lt;210&gt; 5

&lt;211&gt; 366

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (1)..(366)

&lt;400&gt; 5

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tcc ctg aga ctc tcc tgt gca gcg tct gga ttc acc ttc agt agc tat 96  
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
                                     20                                    25                                    30

gac ata cac tgg gtc cgc cag gct cca ggc aag ggg ctg gag tgg gtg  
 144  
 Asp Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
                                     35                                    40                                    45

gca gta ata tgg tat gat ggc agt aat aaa tac cat gca gac tcc gtg  
 192  
 Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr His Ala Asp Ser Val  
          50                                    55                                    60

aag ggc cga ttc acc atc tcc aga gac aat tcc aag aac acg ctg tat  
 240  
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
          65                                    70                                    75                                    80

ctg caa atg aac agt ctg aga gcc gag gac acg gct gtg tat tac tgt  
 288  
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
                                     85                                    90                                    95

gcg aga aac tat ggt ttg ggg agt tat tat aac tac ttt gac ttc tgg  
 336  
 Ala Arg Asn Tyr Gly Leu Gly Ser Tyr Tyr Asn Tyr Phe Asp Phe Trp  
                                     100                                    105                                    110

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 366  
 Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
          115                                    120

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<210> 6  
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 <212> PRT  
 <213> Homo sapiens

<400> 6  
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 Asp Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
 35 40 45  
 Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr His Ala Asp Ser Val  
 50 55 60  
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
 65 70 75 80  
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
 85 90 95  
 Ala Arg Asn Tyr Gly Leu Gly Ser Tyr Tyr Asn Tyr Phe Asp Phe Trp  
 100 105 110  
 Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
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<220>  
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 <222> (1)..(321)

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 gac aga gtc acc atc act tgt cgg gcg agt cat ggt att agc agc tgg 96  
 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser His Gly Ile Ser Ser Trp  
 20 25 30  
 tta gcc tgg tat cag cag aaa cca gag aaa gcc cct aag tcc ctg atc  
 144  
 Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile  
 35 40 45  
 tat gct gca tcc agt ttg caa agt ggg gtc cca tca agg ttc agc ggc

- 6 -

192  
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly  
50 55 60

agt gga tct ggg aca gat ttc act ctc acc atc agc agc ctg cag cct  
240  
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro  
65 70 75 80

gaa gat ttt gca act tat tac tgc caa cag tat aat agt tac ccg tac  
288  
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Tyr  
85 90 95

act ttt ggc cag ggg acc aag ctg gag atc aaa  
321  
Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys  
100 105

<210> 8  
<211> 107  
<212> PRT  
<213> Homo sapiens

<400> 8  
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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser His Gly Ile Ser Ser Trp  
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Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile  
35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly  
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro  
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Tyr  
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys  
100 105

<210> 9  
<211> 366  
<212> DNA  
<213> Homo sapiens

<220>  
<221> CDS

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&lt;222&gt; (1) .. (366)

&lt;400&gt; 9

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 Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg  
 1 5 10 15

tcc ctg aga ctc tcc tgt gca gcg tct gga ttc acc ttc agt agc tat 96  
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
 20 25 30

gtc atg cac tgg gtc cgc cag gct cca ggc aag ggg ctg gag tgg gtg  
 144  
 Val Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
 35 40 45

gca gtt ata tgg tat gat gga agt aat aaa tac tat gca gac tcc gtg  
 192  
 Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val  
 50 55 60

aag ggc cga ttc acc atc tcc aga gac aat tcc aag aac acg ctg tat  
 240  
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
 65 70 75 80

ctg caa atg aac agc ctg aga gcc gag gac acg gct gtg tat tac tgt  
 288  
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
 85 90 95

gcg ctt atg gtt cgg gga ctt att ata acg ggg tac ttt gac tac tgg  
 336  
 Ala Leu Met Val Arg Gly Leu Ile Ile Thr Gly Tyr Phe Asp Tyr Trp  
 100 105 110

ggc cag gga acc ctg gtc acc gtc tcc tca  
 366  
 Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
 115 120

&lt;210&gt; 10

&lt;211&gt; 122

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 10

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg  
 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
 20 25 30

Val Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
 35 40 45

- 8 -

Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val  
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
 85 90 95

Ala Leu Met Val Arg Gly Leu Ile Ile Thr Gly Tyr Phe Asp Tyr Trp  
 100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
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<210> 11

<211> 324

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(324)

<400> 11

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 1 5 10 15

gaa aga gcc acc ctg tcc tgc agg gcc agt cag agt gtt agc agc tac 96  
 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr  
 20 25 30

tta gcc tgg tac caa cag aaa cct ggc cag gct ccc agg ctg ctg atc  
 144

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile  
 35 40 45

tat gat gca tcc aac agg gcc act ggc atc cca gcc agg ttc agt ggc  
 192

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly  
 50 55 60

agt ggg tct ggg aca gac ttc act ctg acc atc agc agc cta gag cct  
 240

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro  
 65 70 75 80

gaa gat ttt gca gtt tat tac tgt cag cag cgt agc aac tgg cct ccg  
 288

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Pro  
 85 90 95

tac act ttt ggc cag ggg acc aag ctg gag atc aaa  
 324



- 9 -

Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys  
                   100                                  105

<210> 12  
 <211> 108  
 <212> PRT  
 <213> Homo sapiens

<400> 12  
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 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr  
                   20                          25                          30  
 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile  
                   35                          40                          45  
 Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly  
           50                          55                          60  
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro  
       65                          70                          75                          80  
 Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Pro  
                           85                          90                          95  
 Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys  
                   100                                  105

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 120  
 aaagcccgtc cattaggcgg gctcttgga gaacatatcc atcgcgctccg ccacttccag  
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 cagccgcacg cggcgcatct cgggcagcgt tgggtcctgg ccacgggtgc gcatgatcgt  
 240  
 gctcctgtcg ttgaggaccc ggctaggctg gcgggggtgc cttactgggt agcagaatga  
 300  
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- 10 -

360

aacaacatga atggtcttcg gtttccgtgt ttcgtaaagt ctggaaacgc ggaagtcagc  
420

gccctgcacc attatgttcc ggatctgcat cgcaggatgc tgctggctac cctgtggaac  
480

acctacatct gtattaacga agcgcctggca ttgaccctga gtgatttttc tctggteccg  
540

ccgcatccat accgccagtt gtttaccctc acaacgttcc agtaaccggg catgttcac  
600

atcagtaacc cgtatcgtga gcatcctctc tcgtttcatc ggtatcatta ccccatgaa  
660

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720

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780

gcggtgaac aggcagacat ctgtgaatcg cttcacgacc acgctgatga gctttaccgc  
840

agctgcctcg cgcgtttcgg tgatgacggg gaaaacctct gacacatgca gctcccgag  
900

acggtcacag cttgtctgta agcggatgcc gggagcagac aagcccgta gggcgcgta  
960

gcgggtgttg gcgggtgtcg gggcgcagcc atgaccagc cagtagcga tagcggagt  
1020

tatactggct taactatgcg gcatcagagc agattgtact gagagtgcac catatgcggt  
1080

gtgaaatacc gcacagatgc gtaaggagaa aataccgcat caggcgtct tccgcttcct  
1140

cgctcactga ctcgctgcgc tcggtcggtc ggctgcggcg agcggatatca gctcactca  
1200

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1260

aaggccagca aaaggccagg aaccgtaaaa aggccgcggt gctggcggtt ttccataggc  
1320

tccgcccccc tgacgagcat cacaaaaatc gacgctcaag tcagaggtgg cgaaaccga  
1380

caggactata aagataccag gcgtttcccc ctggaagctc cctcgtgcgc tctcctgttc  
1440

- 11 -

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1560

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1620

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1740

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1800

tgaagccagt taccttcgga aaaagagttg gtagctcttg atccggcaaa caaaccaccg  
1860

ctggtagcgg tgggtttttt gtttgcaagc agcagattac gcgcagaaaa aaaggatctc  
1920

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1980

aagggatctt ggcatgaga ttatcaaaaa ggatcttcac ctagatcctt ttaaattaaa  
2040

aatgaagttt taaatcaatc taaagtatat atgagtaaac ttggtctgac agttaccaat  
2100

gcttaatcag tgaggcacct atctcagcga tctgtctatt tcgttcaccc atagttgcct  
2160

gactccccgt cgtgtagata actacgatac gggagggcct accatctggc cccagtgcgt  
2220

caatgatacc gcgagaccca cgctcacccg ctccagattt atcagcaata aaccagccag  
2280

ccggaagggc cgagcgcaga agtggtcctg caactttatc cgctccatc cagtctatta  
2340

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ccattgctgc aggcacgtg gtgtcacgct cgtcgtttgg tatggcttca ttcagctccg  
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tggcagcaact gcataattct cttactgtca tgccatccgt aagatgcttt tctgtgactg  
2640

gtgagtactc aaccaagtca ttctgagaat agtgtatgcg gcgaccgagt tgctcttgcc  
2700

cggcgtcaac acgggataat accgcgccac atagcagaac tttaaaagtg ctcatcattg  
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2880

ggtgagcaaa aacaggaagg caaatgccg caaaaaaggg aataagggcg acacggaaat  
2940

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3000

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3060

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3120

ataaaaaatag gcgtatcacg aggccctttc gtcttcaag  
3159